EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Hadassa Waterman and Matrin Moynihan on 2/14/2008.

The application has been amended as follows:

In the claims:

1. (Currently Amended) A method of reducing extracellular brain glutamate levels in a subject in need thereof, the method comprising intravenously administering to the subject a therapeutically effective amount of a glutamate modifying enzyme, thereby enhancing brain to blood glutamate efflux, thereby reducing extracellular brain glutamate levels.

Deleted: capable of reducing blood glutamate levels

2. (Previously Presented) The method of claim 1, wherein said glutamate modifying enzyme is a naturally occurring enzyme.

3. (Previously Presented) The method of claim 1, wherein said at least one glutamate modifying enzyme is selected from the group consisting of a transaminase, a dehydrogenase, a decarboxylase, a ligase, an aminomutase , a racemase and a transferase.

4. (Original) The method of claim 3, wherein said transaminase is selected from the group consisting of glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, acetylornithine transaminase, ornithine-oxo-acid transaminase, succinyldiaminopimelate transaminase, 4-aminobutyrate transaminase, (s)-3-amino-2-methylpropionate transaminase, 4-hydroxyglutamate transaminase, diiodotyrosine transaminase, thyroid-hormone transaminase, tryptophan transaminase, diamine transaminase, cysteine transaminase, L-Lysine 6-transaminase,

histidine transaminase, 2-aminoadipate transaminase, glycine transaminase, branched-chain-amino-acid transaminase, 5-aminovalerate transaminase, dihydroxyphenylalanine transaminase, tyrosine transaminase, phosphoserine transaminase, taurine transaminase, aromatic-amino-acid transaminase, aromatic-amino-acid-glyoxylate transaminase, leucine transaminase, 2-aminohexanoate transaminase, ornithine(lysine) transaminase, kynurenine-oxoglutarate transaminase, D-4-hydroxyphenylglycine transaminase, cysteine-conjugate transaminase, 2,5-diaminovalerate transaminase, histidinol-phosphate transaminase, diaminobutyrate-2-oxoglutarate transaminase, and udp-2-acetamido-4-amino-2,4,6-trideoxyglucose transaminase.

5-9. (Canceled)

10. (Previously Presented) The method of claim 1, further comprising administering to the subject at least one co-factor of a glutamate modifying enzyme.

11. (Original) The method of claim 10, wherein said co-factor is selected from the group consisting of oxaloacetate, pyruvate, NAD^+, $NADP^+$, 2-oxohexanedioic acid, 2-oxo-3-sulfopropionate, 2-oxo-3-sulfinopropionic acid, 2-oxo-3-phenylpropionic acid, 3-indole-2-oxopropionic acid, 3-(4-hydroxyphenyl)-2-oxopropionic acid, 4-methylsulfonyl-2-oxobutyric acid, 3-hydroxy-2-oxopropionic acid, 5-oxopentanoate, 6-oxo-hexanoate, glyoxalate, 4-oxobutanoate, α-ketoisocaproate, α-ketoisovalerate, α-keto-β-methylvalerate, succinic semialdehyde-(-4-oxobutyrate), pyridoxal phosphate, pyridoxal phosphate precursors and 3-oxoisobutanoate.

12. (Previously Presented) The method of claim 1, wherein said glutamate modifying enzyme is an artificially modified glutamate modifying enzyme incapable of converting a glutamate metabolite into glutamate.

13. (Previously Presented) The method of claim 12, wherein said artificially modified glutamate modifying enzyme is an artificially modified human GOT.

14. (Previously Presented) The method of claim 1, further comprising administering to the subject a co-factor of said glutamate modifying enzyme, said glutamate modifying enzyme being artificially modified glutamate modifying enzyme incapable of converting modified glutamate into glutamate.

15. (Previously Presented) The method of claim 14, wherein said co-factor is selected from the group consisting of lipoic acid, lipoic acid precursor, pyridoxal phosphate, pyridoxal phosphate precursor, thiamine pyrophosphate and thiamine pyrophosphate precursor.

16-25. (Canceled)

26. (Previously Presented) The method of claim 1, wherein said administering is effected at a concentration of said enzyme not exceeding 1 g/Kg body weight/hour.

27-119. (Canceled)

16-25. (Canceled)

26. (Previously Presented) The method of claim 1, wherein said administering is effected at a concentration of said enzyme not exceeding 1 g/Kg body weight/hour.

27-119. (Canceled)

120. (Previously Presented) The method of claim 1, wherein said glutamate modifying enzyme is a glutamate oxaloacetate transaminase.

121. (Previously Presented) The method of claim 120, further comprising administering oxaloacetate.

122. (Currently Amended) A method of reducing extracellular brain glutamate levels, the method comprising intravenously administering to a subject in need thereof a therapeutically

effective amount of a glutamate modifying enzyme and a co-factor thereof, thereby enhancing brain to blood glutamate efflux., thereby reducing extracellular brain glutamate levels.

123. (Previously Presented) The method of claim 122, wherein said glutamate modifying enzyme is glutamate oxaloacetate transaminase and said co-factor is oxaloacetate.

124. (Previously Presented) The method of claim 122, wherein said glutamate modifying enzyme is a naturally occurring enzyme.

125. (Previously Presented) The method of claim 122, wherein said glutamate modifying enzyme is an artificially modified glutamate modifying enzyme incapable of converting a glutamate metabolite into glutamate.

126-130. (Cancelled)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIFFANY M. GOUGH whose telephone number is (571)272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Tiffany M Gough/
Examiner, Art Unit 1657

/Ruth A. Davis/

Primary Examiner, Art Unit 1651